# Homeopathic Product Regulation: Evaluating FDA's Regulatory Framework After a Quarter-Century April 20, 2015

Testimony of
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Good morning. I'm Adriane Fugh-Berman, Associate Professor, Dept. of Pharmacology and Physiology, Georgetown University Medical Center, where I teach about medicinal plants, dietary supplements, and evidence-based medicine. I direct PharmedOut, a project that promotes rational prescribing. I have no commercial conflicts of interest. I'm a paid expert witness in litigation regarding pharmaceutical marketing practices. I have authored two books on complementary medicine, written the first chapter on CAM in *Harrison's Principles of Internal Medicine* and have worked for the Office of Alternative Medicine (now the National Center for Complementary and Integrative Health). Between 1998 and 2012, I consulted with the FTC on dietary supplements.

I am concerned about the current state of labeling for homeopathic remedies, particularly OTC preparations. Although the FDA has increased its focus on the safety, quality, and claims of dietary supplements (products that are not permitted to make "disease" claims), the agency has continued to defer its regulatory oversight of homeopathic drugs.

In the US, both classical homeopathy and homeopathic polypharmacy are practiced. Classical homeopathy looks for a precise match between a patient's symptoms and temperament and a single remedy – an early form of personalized medicine. The sequestered racks of individual homeopathic remedies, ordered or compounded by prescription, and administered by those with specialized knowledge, have not and should not be a regulatory concern.

The majority of homeopathic drugs sold OTC to consumers today, however, represent ingredient mixtures, or polypharmacy. For example, 21C Natural Remedies Remedy No. 11 for "ADD and ADHD" contains no fewer than 22 HPUS (Homeopathic Pharmacopoeia of the U.S.) ingredients.

Stocking homeopathic remedies labeled for specific symptoms or conditions alongside conventional OTC drugs on the pharmacy or supermarket shelves is innately misleading. Most consumers have no idea what homeopathy is and may assume that these products are dietary supplements or even conventional drugs. Consumers (and, probably, most health professionals) are unaware that FDA does not review homeopathic drugs for safety or efficacy. And while homeopathic drugs are supposed to comply with federal requirements for good manufacturing practices (GMPs), it is my understanding that FDA does not routinely review these products for identity, purity, potency, quality or stability prior to marketing.

### Safety Is Not A Given

It is generally believed that homeopathic drugs are completely safe because they are highly diluted. Homeopaths believe that the more a remedy is ritually diluted, the more potent the remedy becomes. From a homeopathic perspective, less diluted remedies are thus considered less potent., and more-diluted remedies are more potent. Thus, "high-potency" or "prescription" homeopathic remedies represent the most dilute forms; these can be assumed safe because any homeopathic preparation

diluted to 30X or beyond (i.e., thirty 10:1 dilutions) is unlikely to have even a single molecule of the original substance left in it. However, most OTC homeopathic remedies are "low-potency" preparations. Because they are not highly dilute, these preparations may contain measurable and pharmacologically active levels of ingredients.

For example, Cold-Eeze® [ProPhase Labs, Inc., PA], an OTC homeopathic cold remedy, contains 13.3 mg of zinc per lozenge¹. At the recommended 6 lozenges a day, that's about 80 mg/zinc daily, or ten times the RDA for adult females, and 8 times the RDA for males.

A similar OTC cold remedy, Zicam® (Matrixx Initiatives, Inc. NJ) states that each lozenge contains Zincum aceticum and Zincum gluconicum at "2X",² representing a dilution of 1 to  $10^2$  (1:100), or 1% concentration. What consumer—or health professional—knows what this nomenclature or dose information means? In this case the drug label provides no useful information to an average consumer or clinician. And those who can interpret the concentration still won't know how many milligrams of zinc are in the product.

Although zinc is an essential element, excessive zinc can can suppress copper and iron absorption and cause other toxic effects. <sup>3</sup> Adverse effects caused by some Zicam products have resulted in litigation<sup>4</sup> and an FDA Warning Letter<sup>5</sup> to this company.

The previously mentioned 21C Natural Remedies Remedy No. 11 for "ADD and ADHD" claims: "Our formulas follow a strict method of herbal extraction to deliver bioavailable active ingredients without any negative side effects." If the ingredients are "bioavailable" they must be in measurable quantities, and not as dilute as the site name "21C" implies.

### Any Ingredient, including Prescription Drugs, can be Homeopathic

Since any ingredient with a homeopathic "proving" that is listed in HPUS qualifies as a homeopathic ingredient, homeopathic remedies can contain arsenic, snake venom, heavy metals, controlled substances and other ingredients that would be considered potentially unsafe by usual drug standards.

<sup>&</sup>lt;sup>1</sup>http://www.coldeeze.com/medical-info/

<sup>&</sup>lt;sup>2</sup> http://www.zicam.com/our-products/cold-shortening/oral-mist-arctic-mint.php

<sup>&</sup>lt;sup>3</sup> Fosmire, G: Zinc toxicity. American Journal of Clinical Nutrition 51:225-7, 1990.

<sup>&</sup>lt;sup>4</sup> USA Today *Homeopathic medicine company fights off Zicam lawsuits* 2007: <a href="http://usatoday30.usatoday.com/money/industries/health/2007-08-01-zicam">http://usatoday30.usatoday.com/money/industries/health/2007-08-01-zicam N.htm</a>

<sup>&</sup>lt;sup>5</sup> FDA Advises Consumers Not To Use Certain Zicam Cold Remedies *Intranasal Zinc Product Linked to Loss of Sense of Smell June 16, 2009* http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm167065.htm

Even more concerning are companies that sell cytokines and other prescription drugs as homeopathic preparations. For example, GUNA Interleukin Remedies® (Forrest Health, Los Gatos, CA; Manufactured by Guna - Milan, Italy) contains IL-2 through IL12, and other cytokines, such as IFN-alfa. Interleukin-2 and Alfa Interferon are prescription drugs approved only for serious conditions; each has significant label warnings and precautions. The homeopathic OTC version is labeled for "Chronic Pain Relief, Anti-inflammatory, Good for Auto Immune." GUNA IL-12 is advertised for "Anti-Allergy Immune Support, Asthma, COPD, Bronchitis."

Another product, King Bio Homeopathic Allergy and Toxicity Food Additives Preservatives™ [Ashville, NC] contains over a dozen ingredients in a "bioenergetically enhanced pure water base." This product is used to counteract "gastrointestinal upset, muscle weakness, nasal congestion, difficult sleeping, hyperactivity, headaches, hives, itching, irritability" due to food additives and preservatives, with dosing for infants, including newborns.<sup>7</sup>

The dangers of selling prescription drugs as homeopathic remedies are obvious.

# It is misleading to sell homeopathic remedies alongside conventional OTC drugs

Allowing homeopathic remedies to sit side-by-side with conventional drugs that have undergone FDA scrutiny as over-the-counter drugs is inherently misleading.

Many consumers have no idea what homeopathy is, and may assume that homeopathic products are phytomedicines or dietary supplements. Not only do homeopathic remedies undergo none of the FDA review that conventional drugs are subject to, but they are not regulated even to the degree that dietary supplements are. Disease claims are disallowed for dietary supplements, but homeopathic remedies can make the same disease treatment claims as conventional drugs!

Perhaps homeopathic remedies should be sequestered from other remedies and sold under a banner or label that explains what homeopathy is, with enough information so that a consumer can make an educated decision about purchasing a remedy that may contain no active compounds.

#### Clinical Evidence is Lacking

Lastly, the evidence for homeopathy's effectiveness is between scant and nil; this picture has become much more clear over the past 20 years. Although Kleijnen's

<sup>6</sup> http://www.forresthealth.com/GUNA-Interleukin.html

<sup>&</sup>lt;sup>7</sup> http://www.kingbio.com/meet-dr-king; http://www.vitacost.com/King-Bio-Homeopathic-Allergy-and-Toxicity-Food-Additives-Preservatives

1991 BMJ paper found that the majority of 105 homeopathy trials were positive, it noted that most trials were of poor methodological quality. Shang's 2005 Lancet analysis compared 110 homeopathy trials with matched trials of conventional medicine, and found only a weak effect of homeopathy, compared to a strong effect of conventional medicine. Benefits attributed to homeopathy-- but not conventional medicine-- disappeared when the analysis was restricted to high-quality trials. And just this year, an assessment of 176 studies in 57 systematic reviews from Australia's National Health and Medical Research Council concluded that "that there are no health conditions for which there is reliable evidence that homeopathy is effective."

# **History and Future Directions**

The inclusion of the Homeopathic Pharmacopeia of the US in the Food Drug and Cosmetic Act of 1938 is often considered a concession to Senator Royal Copeland, a surgeon and homeopathic physician, but the FDA's own historian, Suzanne Junod, has pointed out that explanation is too simplistic. An accomplished surgeon, Copeland did not consider homeopathy a system of medicine. He considered homeopathy a complementary, not an alternative therapy, and was not actively promoting homeopathy at that time in his career. At the time, homeopathy was practiced by physicians and the medical profession was not hostile to this practice. In fact, there were more homeopathic physicians in the AMA than in the American Institute of Homeopathy; the AMA, with Morris Fishbein at its helm, did not oppose the inclusion of the Homeopathic Pharmacopeia in the 1938 act. Junod suggests that the inclusion of a physician-prescribed class of therapies was an effort to combat fraudulent therapies that were widely sold. While physicians could be held to a code of ethics, charlatans could not. Perhaps the belief that homeopathy was a dying specialty also played a role in the AMA's passivity.

In 1972, the FDA decided to exclude homeopathic products from FDA drug review. The market was considered trivial, the products lacked safety concerns, and – once again – homeopathy was considered a dying specialty. While its popularity waxes and wanes, reports of homeopathy's demise have been greatly exaggerated. Ironically, the presence of quack remedies on the market may have contributed to the inclusion of the Homeopathic Pharmacopeia in the 1938 act. We need to invoke that spirit once more.

<sup>&</sup>lt;sup>8</sup> Kleijnen J, Knipschild P, ter Riet G. Clinical trials of homoeopathy. BMJ. 1991 Feb 9;302(6772):316-23.

<sup>&</sup>lt;sup>9</sup> Shang A, Huwiler-Müntener K, Nartey L, Jüni P, Dörig S, Sterne JA, Pewsner D, Egger M. Are the clinical effects of homoeopathy placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. Lancet. 2005 Aug 27-Sep 2;366(9487):726-32.

<sup>&</sup>lt;sup>10</sup> National Health and Medical Research Council. NHMRC Statement on Homeopathy - Evidence on the effectiveness of homeopathy for treating health conditions. 2015 (March). Available at: https://www.nhmrc.gov.au/guidelines-publications/cam02 NHMRC INFORMATION PAPER Evidence on the effectiveness of homeopathy for treating health conditions. 2015 (March). Available at https://www.nhmrc.gov.au/ files nhmrc/publications/attachments/cam02a information paper.pdf

<sup>&</sup>lt;sup>11</sup> Junod SW. An alternative perspective: homeopathic drugs, Royal Copeland, and federal drug regulation. Food Drug Law J. 2000;55(1):161-83.

# Homeopathic remedies should have to disclose their ingredients using modern nomenclature and standard dosing terms.

The FDA must reconsider its deferral of regulation over homeopathic drugs. All OTC preparations should have to disclose ingredients on the label and how much of each active ingredient they contain. I propose the following recommendations in order to improve the OTC homeopathic drug label:

- All active ingredients should be listed using modern chemical, scientific, language, as FDA currently requires for drugs, foods, and dietary supplements. For plant products, Latin binomial nomenclature, common name, and plant part should be included.,
- All inactive ingredients should be listed, using the same principles as required for conventional drugs.
- Ingredient quantities should be expressed in standard scientific format, e.g., micrograms per tablet, milligrams per milliliter, etc. not just homeopathic dilution formats.
- Any use/indication that would fall under prescription status should be submitted under a New Drug Application (NDA) and be reviewed and approved by FDA for product consistency and quality, safety and efficacy, using standard study designs, prior to marketing in the United States.
- If the FDA decides to continue its deferral of regulatory oversight on homeopathic remedies, then it is strongly recommended that a disclaimer be added to the OTC homeopathic remedy label, to the effect: "This product is a homeopathic remedy. As such it has not undergone review or approval by the FDA and, therefore, has not been documented to be safe or effective to diagnose, treat, prevent, mitigate or cure any condition or disease."

To date, the lack of regulation of homeopathy has depended on its safety, but it is not safe to have mislabeled, misleading products on the shelves.

Thank you.